What is claimed is:

1. A nucleic acid composition for muting expression of a gene with unwanted activity in an animal cell, wherein the muting nucleic acid includes a sequence homologous to an endogenous sequence in the gene.

2. A nucleic acid composition according to claim 1, wherein the gene with unwanted activity is carried on a chromosome of the cell.

3. A nucleic acid composition according to claim 1, wherein the cell is selected from the group consisting of a cancer cell, an autoimmune cell, and a cell having a gene of a pathogen.

4. A nucleic acid composition according to claim 3, wherein the pathogen is a virus.

5. A nucleic acid composition according to claim 1, wherein the nucleic acid is selected from the group consisting of a DNA, an RNA, and a nucleic acid analog.

6. A nucleic acid composition according to claim 5, wherein the nucleic acid analog is selected from the group consisting of a phosphorothioate, a 2'-*o*-methyl RNA, and a peptide nucleic acid.

7. A nucleic acid composition according to claim 1, wherein the nucleic acid is double stranded DNA.

8. A nucleic acid composition according to claim 1, wherein the animal is a vertebrate.

9. A nucleic acid composition according to claim 8, wherein the vertebrate is a

warm-blooded animal.

10. A nucleic acid composition according to claim 9, wherein the warm-blooded animal is a mammal.

11. A method for muting expression of an endogenous gene having unwanted activity in a cell of an animal, the method comprising the steps of:

(a) providing a muting nucleic acid; and

(b) delivering the muting nucleic acid into the cell.

12. A method according to claim 10, wherein providing the muting nucleic acid includes providing a nucleic acid composition having a transgene, the transgene having a sequence that is substantially homologous to a sequence in the endogenous gene with unwanted activity.

13. A method according to claim 11, wherein the nucleic acid is selected from the group consisting of DNA, RNA, and a nucleic acid analog.

14. A method according to claim 13, wherein (a) further comprises the step of engineering the nucleic acid into a recombinant vector.

15. A method according to claim 14, wherein the recombinant vector is a plasmid, a phagemid, or a virus.

16. A method according to claim 15, wherein the vector is a double-stranded DNA plasmid.

17. A method according to claim 12, wherein the muting transgene sequence is substantially homologous to an endogenous sequence that extends to a portion of the

endogenous gene selected from at least one of the group of: the 5' untranscribed portion, the transcribed coding portion including introns, the 3' untranslated portion, the 3' untranscribed portion, and a portion that overlaps adjacent ends of at least two portion of the endogenous gene.

18. A method according to claim 17, wherein the nucleic acid comprises a sequence that is substantially homologous to an endogenous sequence located in the 5' portion of the endogenous gene.

19. A method according to claim 18, wherein the endogenous sequence located in the 5' portion comprises about 200 to about 400 bases in length.

20. A method according to claim 18, wherein the endogenous sequence located in the 5' portion comprises about 400 to about 600 bases in length.

21. A method according to claim 18, wherein the endogenous sequence located in the 5' portion comprises about 600 to about 1,000 bases in length.

22. A method according to claim 11, wherein the muting nucleic acid comprises a sequence that is substantially homologous to an endogenous sequence located at the 3' portion of the gene having unwanted activity.

23. A method according to claim 22, wherein the 3' portion of the gene includes an untranscribed portion and a portion that overlaps the 3' end of the coding portion.

24. A method according to claim 11, wherein the step of delivering the muting nucleic acid in (b) is selected from the group of: transforming, transfecting, electroporating, infecting, and lipofecting the nucleic acid into the cell.

25. A method according to claim 24, wherein delivering the muting nucleic comprises infecting the cell with a genetically attenuated bacterium or virion.

26. A method according to claim 16, wherein following (b), the plasmid is not substantially integrated into a chromosome.

27. A method according to claim 26, wherein the plasmid is transiently maintained in the cell.

28. A method for identifying a muting nucleic acid that reduces expression of an endogenous target gene having unwanted activity in cells of an animal, comprising the steps of:

(a) providing a set of fragments of DNA encoding the target gene, wherein the fragments are engineered into a plurality of vector molecules to produce a recombinant vector library;

(b) delivering the vector library into the cells, to form a plurality of transgenic cloned fragment recipients; and

(c) comparing expression of the target gene in each of a subset of the cloned recipients, to expression of the target gene in the cells of the animal, to identify a cloned recipient having a vector with the muting nucleic acid, wherein expression of the target gene is reduced.

29. A method according to claim 28, wherein the animal is warm-blooded.

30. A method according to claim 29, wherein the animal is a mammal.

31. A method according to claim 28, wherein the vector carries also a chemical resistance gene conferring a phenotype which is ability to grow in the presence of the chemical.

32. A method according to claim 31, having an additional step of:

(a) comparing expression of the resistance gene in the cell having the muting nucleic acid, with expression of the resistance gene in the animal cell.

33. A method according to claim 32, wherein the resistance gene is selected from the group consisting of *AMP* and *CAT*, encoding encoding β-lactamase and chloramphenicol acetyl transferase, respectively.

34. A method according to claim 28, having a further step:

(a) comparing expression of a second endogenous gene which is not the target gene in the cell having a muting nucleic acid, with expression of the second endogenous gene in the animal cell.

35. A method according to claim 34, wherein the second endogenous gene is *GADPH*, encoding glyceraldehyde-3-phosphate dehydrogenase.

36. A method of evaluating a phenotype of animal cells engineered to mute expression of a target endogenous gene, comprising:

(a) transforming animal cells capable of expressing the target gene with the vector having the muting nucleic acid obtained according to the method of claim 28; and

(b) observing the transformed cells for an altered phenotype in comparison to the parental animal cells capable of expressing the target gene.

37. A method according to claim 36, wherein the altered phenotype under a set of specified conditions is selected from the group consisting of an alteration of: growth rate, nutritional requirement, contact inhibition among confluent cells, formation of foci, presence of a receptor for a ligand, signal transduction in response to an effector molecule, sensitivity to a pathogen, expression of a developmental protein, and cell cycle pattern.

38. A method according to claim 37, wherein the altered phenotype is cessation of growth or colony formation under specified conditions different from the conditions for growth of the parental animal cells capable of expressing the target gene.

39. A method according to claim 37, wherein the specified conditions different from the conditions for growth of the parental animal cells capable of expressing the target gene comprise at least one of the conditions selected from the group of: an elevated temperature, a depressed temperature, a decreased serum concentration, an elevated serum concentration, a decreased carbon dioxide concentration, an increased carbon dioxide concentration, an increased density of plating, and a decreased density of plating.

40. A method according to claim 37, wherein the altered phenotype is cessation of growth or colony formation under specified conditions that are the same as the conditions for growth of the parental animal cells capable of expressing the target gene.

41. A method according to claim 37, wherein the animal cells are present in an embryonic or postnatal animal.

42. A method of screening a plurality of molecules to obtain a composition capable of muting expression of an endogenous gene in cells of a cell line, comprising:

mixing a subset of each of the plurality of molecules with a plurality of samples of the cells, to produce a plurality of test cell cultures;

providing a nucleic acid capable of muting expression of the gene;

transforming the nucleic acid into a sample of the cells, to produce a positive control cell culture having muting of expression of the endogenous gene; and

detecting an amount of expression of the endogenous gene in each of the test cell cultures in comparison with the positive control cell culture and with untreated cells of the cell line, such that a test cell culture with substantially reduced expression of the gene compared to expression in the untreated cells, and substantially equivalent expression

compared to cells in the positive control culture, identifies the composition capable of muting expression of the gene.

43. A method according to claim 42, wherein detecting expression of the endogenous gene comprises analyzing cell RNA by hybridization with a probe.

44. A method according to claim 43, wherein the hybrid of the cell RNA and the probe is digested with RNase.

45. A method according to claim 44, the digested RNA is submitted to gel electrophoresis to determine the size of the cell RNA protected from RNase digestion by the probe.

46. A method according to claim 42, wherein detecting expression of the endogenous gene comprises detecting a color change or absence of a color change in the cells.

47. A method according to claim 46, wherein the color change in the cells is indicative of expression of the endogenous gene which has been fused to a second gene having a colorimetric assay.

48. A method according to claim 42, wherein the molecules are selected from the group consisting of extracts of natural product fermentations and synthesized organic chemicals.

49. A method according to claim 48, wherein the organic chemicals are synthesized according to combinatorial methods.

50. A composition obtained by the method of claim 42 in a pharmaceutically

acceptable carrier.

51. A method of screening a plurality of molecules to obtain a composition capable of alleviating muting of expression of an endogenous gene in cells of a cell line having a muted endogenous gene, comprising:

mixing a subset of each of the plurality of molecules with a plurality of samples of the cells having the muted endogenous gene, to produce a plurality of test cell cultures; and

detecting amounts of expression of the endogenous gene in each of the test cell cultures in comparison with the cells of the cell line having the muted endogenous gene, and in untreated cells of a parental cell line in which the endogenous gene is not muted, such that a test cell culture with expression of the gene that is substantially greater than the expression in the cell line having the muted endogenous gene, and that is substantially equivalent to expression in cells of the parental non-muted culture, identifies the composition capable of alleviating muting of expression of the gene.

52. A composition identified by the method of claim 51, in a pharmaceutically acceptable carrier.

53. A kit for identifying a muting nucleic acid that reduces expression of an endogenous gene, the kit comprising reagents for assaying quantitatively both protection of a riboprobe from ribonuclease digestion, and amount of transfected DNA.

54. A kit according to claim 53, wherein the reagents comprise chemicals, stabilized enzymes, and buffers.

55. A kit according to claim 53, wherein the reagents comprise diethylpyrocarbonate-treated water, placental RNase inhibitor, tRNA, a buffer containing piperazine-*N,N'*-bis(2-ethanesulfonic acid), a DNase I digestion buffer, phenylmethylsulfonyl

fluoride, and gelatin.

56. A kit according to claim 54, wherein the stabilized enzymes comprise: an RNA polymerase selected from the group of SP6 RNA polymerase and T7 RNA polymerase; a ribonuclease selected from the group of RNase I and a mixture of RNases A and T_1; *Taq* polymerase; proteinase K; and DNase-free pancreatic RNase.

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